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     (FILE 'HOME' ENTERED AT 13:41:05 ON 19 FEB 2003)

     FILE 'MEDLINE' ENTERED AT 13:42:47 ON 19 FEB 2003
L1             0 S BOROWSKY/AU AND MCH
L2            15 S BOROWSKY B/AU
L3            13 S BLACKBURN T/AU
L4             0 S OGOZALEK K/AU
L5             0 S (L2 OR L3) AND MCH
L6            28 S L2 OR L3
L7             0 S L6 AND MCH
L8          2090 S MCH OR (MELANIN (W) CONCENTRATING (W) HORMONE)
L9            82 S L8 AND (DEPRESSION OR STRESS OR ANXIETY OR PSYCHOTIC OR NEURO
L10           74 S L8 (P) (DEPRESSION OR STRESS OR ANXIETY OR PSYCHOTIC OR NEURO
L11           69 S L8 (P) (DEPRESSION OR STRESS OR ANXIETY OR ANXIOLYTIC)
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	Type	L #	Hits	Search Text	DBs	Time Stamp
1	BRS	L1	111	BOROWSKY.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/02/19 11:04
2	BRS	L7	1261	Blackburn.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/02/19 11:05
3	BRS	L13	6	Ogozalek.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/02/19 11:05
4	BRS	L19	3	(L1 or L7 or L13) and (MCH)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/02/19 11:34
5	BRS	L25	1525	MCH or (melanin adj concentrating adj hormone)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/02/19 13:34
6	BRS	L31	279	L25 and (depression or stress or anxiety or psychotic or neurological or anxiolytic)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/02/19 13:35

	Type	L #	Hits	Search Text	DBs	Time Stamp
7	BRS	L37	242	L25 and (depression or stress or anxiety or anxiolytic)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/02/19 13:35
8	BRS	L43	30	L25 same (depression or stress or anxiety or anxiolytic)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/02/19 13:36

	U	1	Document ID	Issue Date	Pages
1	☒	☐	US 20030027252 A1	20030206	49
2	☒	☐	US 20030023085 A1	20030130	27
3	☒	☐	US 20020198232 A1	20021226	33
4	☒	☐	US 20020156095 A1	20021024	18
5	☒	☐	US 20020111306 A1	20020815	66
6	☒	☐	US 20020046054 A1	20020418	22
7	☒	☐	US 6413982 B1	20020702	37
8	☒	☐	US 6383136 B1	20020507	7
9	☒	☐	US 6369053 B1	20020409	17

	Title	Current OR	Current XRef	Retrieval Classif
1	Novel receptors	435/69.1	435/320.1; 435/325; 530/350; 536/23.5	
2	Fused heterocyclic compounds	544/14	544/233; 544/99; 546/62; 546/70; 549/23; 549/383	
3	4-substituted quinoline derivatives	514/314	546/167	
4	2-aminoquinolinecarboxamides: neurokinin receptor ligands	514/311	546/168	
5	DNA encoding a human melanin concentrating hormone receptor (MCH1) and uses thereof	514/12	435/320.1; 435/325; 435/69.1; 530/350; 536/23.5	
6	Use of blood and plasma donor samples and data in the drug discovery process	705/1	700/1	
7	4-substituted quinoline derivatives	514/314	514/312; 514/313; 546/153; 546/159; 546/167	
8	Health analysis and forecast of abnormal conditions	600/300	128/920; 705/3	
9	2-Aminoquinolinecarboxamides: neurokinin receptor ligands	514/228.2	514/235.2; 514/278; 514/307; 514/313; 544/128; 544/62; 546/144; 546/156; 546/160; 546/161; 546/169; 546/19	

	Inventor	S	C	P	2	3	4	5	Image Doc. Displayed	PT
1	Tian, Hui et al.	☐	☐	☐	☐	☐	☐	☐	US 20030027252	☐
2	Chen, Xiaoqi et al.	☐	☐	☐	☐	☐	☐	☐	US 20030023085	☐
3	Yuan, Jun et al.	☐	☐	☐	☐	☐	☐	☐	US 20020198232	☐
4	Yuan, Jun et al.	☐	☐	☐	☐	☐	☐	☐	US 20020156095	☐
5	Salon, John A. et al.	☐	☐	☐	☐	☐	☐	☐	US 20020111306	☐
6	Morand, Patrick G. et al.	☐	☐	☐	☐	☐	☐	☐	US 20020046054	☐
7	Yuan, Jun et al.	☐	☐	☐	☐	☐	☐	☐	US 6413982	☐
8	Jordan, Charlyn	☐	☐	☐	☐	☐	☐	☐	US 6383136	☐
9	Yuan, Jun et al.	☐	☐	☐	☐	☐	☐	☐	US 6369053	☐

	U	1	Document ID	Issue Date	Pages
10	☒	☐	US 6291195 B1	20010918	42
11	☒	☐	US 6221616 B1	20010424	36
12	☒	☐	US 6221613 B1	20010424	42
13	☒	☐	US 5817631 A	19981006	27
14	☒	☐	US 5776968 A	19980707	26
15	☒	☐	US 5703051 A	19971230	26
16	☒	☐	US 5530095 A	19960625	14

	Title	Current OR	Current XRef	Retrieval Classif
10	DNA encoding a human melanin concentrating hormone receptor (MCH1) and uses thereof	435/7.21	435/252.3; 435/320.1; 435/336; 435/357; 435/361; 435/365; 435/366; 435/7.1; 435/7.2; 530/350; 536/23.5	
11	DNA encoding a human melanin concentrating hormone receptor (MCH1) and uses thereof	435/7.1	435/325; 435/348; 435/356; 435/357; 435/361; 435/365; 435/366; 435/372; 530/350; 536/23.5	
12	DNA encoding a human melanin concentrating hormone receptor (MCH1) and uses thereof	435/7.1	435/325; 435/348; 435/356; 435/357; 435/361; 435/365; 435/366; 435/372; 514/2; 530/350; 536/23.5	
13	Therapeutic uses of melanin	514/21	424/195.11; 424/94.4; 514/567; 514/64	
14	Therapeutic uses of melanin	514/414	514/12; 514/415	
15	Therapeutic uses of melanin	514/21	424/195.11; 424/94.4; 514/567; 514/63	
16	Peptides of melanin concentrating hormone precursor	530/326	435/69.4; 530/327; 530/395	

	Inventor	S	C	P	2	3	4	5	Image Doc. Displayed	PT
10	Salon, John A. et al.	☐	☐	☐	☐	☐	☐	☐	US 6291195	☐
11	Salon, John A. et al.	☐	☐	☐	☐	☐	☐	☐	US 6221616	☐
12	Salon, John A. et al.	☐	☐	☐	☐	☐	☐	☐	US 6221613	☐
13	Berliner, David L. et al.	☐	☐	☐	☐	☐	☐	☐	US 5817631	☐
14	Berliner, David L. et al.	☐	☐	☐	☐	☐	☐	☐	US 5776968	☐
15	Berliner, David L et al.	☐	☐	☐	☐	☐	☐	☐	US 5703051	☐
16	Vaughn, Joan et al.	☐	☐	☐	☐	☐	☐	☐	US 5530095	☐

	U	1	Document ID	Issue Date	Pages
17	☒	☐	US 5449766 A	19950912	16
18	☒	☐	US 5210076 A	19930511	27
19	☒	☐	US 5049655 A	19910917	14
20	☒	☐	US 4500530 A	19850219	7
21	☒	☐	US 4383997 A	19830517	9
22	☒	☐	US 4202033 A	19800506	
23	☒	☐	US 4167038 A	19790904	
24	☒	☐	WO 200208290 A	20020131	
25	☒	☐	WO 200206245 A	20020124	

	Title	Current OR	Current XRef	Retrieval Classif
17	DNA encoding NEI and NGE peptides	536/23.5	435/252.3; 435/320.1; 435/69.1; 435/69.4; 530/300; 530/326; 536/22.1; 536/23.1	
18	Methods of treating Parkinson's disease using melanin	514/21	424/195.16; 424/94.4; 514/567	
19	Melanin-concentrating hormones	530/326	435/320.1; 435/69.4; 530/827; 530/854; 536/23.51	
20	Method of treating horses to inhibit or reduce increases in crenated red blood cells during exercise	514/255.04		
21	Method of treating horses to inhibit or reduce increases in crenated red blood cells during exercise	514/255.04	514/263.36	
22	Apparatus and method utilizing calculator for quality control of hematology sample analysis	436/183		
23	Calculated parameter generation in a hematology parameter measurement apparatus	600/368	377/12; 702/26	
24	New dog MCH receptor polypeptides and nucleic acids, useful for achieving weight loss or gain, treating cancer (e.g. colon or breast), reducing pain or stress, or treating sexual dysfunction			
25	New pyrimidine derivatives are melanin concentrating hormone receptor-1 (MCH-1) antagonists, useful for the treatment of e.g. depression and anxiety and for the modulation of feeding behaviors			

	Inventor	S	C	P	2	3	4	5	Image Doc. Displayed	PT
17	Vaughan, Joan et al.	☐	☐	☐	☐	☐	☐	☐	US 5449766	☐
18	Berliner, David L. et al.	☐	☐	☐	☐	☐	☐	☐	US 5210076	☐
19	Vaughan, Joan et al.	☐	☐	☐	☐	☐	☐	☐	US 5049655	☐
20	Boucher, John H.	☐	☐	☐	☐	☐	☐	☐	US 4500530	☐
21	Boucher, John H.	☐	☐	☐	☐	☐	☐	☐	US 4383997	☐
22	Strobel, Stanley W.	☐	☐	☐	☐	☐	☐	☐		☐
23	Hennessy, James W.	☐	☐	☐	☐	☐	☐	☐		☐
24	TAN, C P	☐	☐	☐	☐	☐	☐	☐		☐
25	CHIU, G et al.	☐	☐	☐	☐	☐	☐	☐		☐

	U	1	Document ID	Issue Date	Pages
26	☒	☐	WO 200187834 A	20011122	
27	☒	☐	WO 200105947 A	20010125	
28	☒	☐	WO 200075166 A	20001214	
29	☒	☐	WO 9850037 A	19981112	
30	☒	☐	EP 514125 A	19921119	

	Title	Current OR	Current XRef	Retrieval Classif
26	Use of new and known amine derivatives as melanin concentrating hormone antagonists for treating e.g. obesity, diabetes, hypertension and arteriosclerosis			
27	Melanin-concentrating hormone receptor polypeptides for increasing or decreasing appetite, reducing stress and to screen for compounds that bind to the receptor			
28	Use of melanin concentrating hormone receptor for identifying MCH receptor agonist or antagonist, receptor ligand, and an individual susceptible to the receptor-associated conditions such as memory disorders			
29	Anxiolytic comprises (2,3-d)thieno:pyrimidine derivative - are used to treat neurotic, stress related and physically manifested disorders			
30	Compsns. comprising triazolo:benzodiazepine(s) - are CCK and gastrin antagonists for treating panic, anxiety and on colonic disorders, pain and withdrawal			

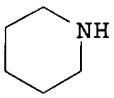
	Inventor	S	C	P	2	3	4	5	Image Doc. Displayed	PT
26	ASO, K et al.	☐	☐	☐	☐	☐	☐	☐		☐
27	HOWARD, A D	☐	☐	☐	☐	☐	☐	☐		☐
28	CIVELLI, O et al.	☐	☐	☐	☐	☐	☐	☐		☐
29	EGUCHI, J et al.	☐	☐	☐	☐	☐	☐	☐		☐
30	BOCK, M G et al.	☐	☐	☐	☐	☐	☐	☐		☐

hydroxy, thiol, CORa, CO2Ra, -ZNR11R12 (Z = bond, cyclo(alkylene)), alkyl, hydroxyalkyl, haloalkyl, alkoxy, fluoroalkoxy or alkoxy substituted by a alkoxy or hydroxyl group (R11 = H, alkyl, cycloalkyl, cycloalkylalkyl, alkyl substituted by alkoxy or hydroxyl group, five or six membered N heterocycle; R12 = H, alkyl, cycloalkyl, cycloalkylalkyl, alkyl substituted by alkoxy or hydroxyl group); R8 = hydrogen, alkyl, fluoroalkyl, hydroxy, alkoxy, hydroxyalkyl; R9 or R10 = H, halo, alkyl, oxo, CO2Ra, CONRaRb, CH2ORc (Rc = H, alkyl, phenyl); n = 0, 1 or 2] and **pharmaceutically** acceptable salts thereof were prepd. as neurokinin 1 (NK-1) receptor antagonists. Thus, tetrahydropyran II (R = Me2N) was prepd. via nucleophilic substitution of the corresponding mesylate II (R = MeSO2O). The compds. are of particular use in the treatment or prevention of **depression**, anxiety, pain, inflammation, migraine, emesis or postherpetic neuralgia (no data).

IT **110-89-4**, Piperidine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of substituted tetrahydropyrans as neurokinin 1 (NK-1) receptor antagonists)

RN 110-89-4 CAPLUS

CN Piperidine (7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L49 ANSWER 25 OF 31 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:412296 CAPLUS

DOCUMENT NUMBER: 133:115233

TITLE: Recent advances in neurokinin-3 receptor antagonists

AUTHOR(S): Giardina, Giuseppe A. M.; Grugni, Mario; Raveglia, Luca F.

CORPORATE SOURCE: Department of Medicinal Chemistry, SmithKline Beecham SpA, Milan, 20021, Italy

SOURCE: Expert Opinion on Therapeutic Patents (2000), 10(6), 939-960
CODEN: EOTPEG; ISSN: 1354-3776

PUBLISHER: Ashley Publications Ltd.

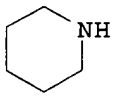
DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review, with 117 refs., of recent highlights and progress made in the neurokinin-3 (NK-3) receptor area since 1997. Whereas in the neurokinin-1 (NK-1) and neurokinin-2 (NK-2) biol. areas literature information based on clin. data account for a high therapeutic potential (in emesis and **depression** for NK-1 and asthma for NK-2 receptor antagonists), there is a total deficiency of information from NK-3 receptor antagonists in clin. development. No other chem. classes in addn. to dichlorophenylalkylpiperidines, represented by SR 142,801 and quinolines, represented by SB-222200 and SB-223412, have been identified by **pharmaceutical** companies and scientists involved in the specific field. Biol. evidence indicates pain/inflammation as a suitable CNS-related therapeutic target, this conclusion is based on localization studies and efficacy of selected NK-3 receptor antagonists in rat disease models of inflammatory pain. In the periphery, the most likely therapeutic indications might be pulmonary and gastrointestinal tract diseases. It is clearly still premature to anticipate any therapeutic potential in man.

IT **110-89-4D**, Piperidine, dichlorophenylalkyl derivs., biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neurokinin-3 receptor antagonists therapeutic potential)
RN 110-89-4 CAPLUS
CN Piperidine (7CI, 8CI, 9CI) (CA INDEX NAME)



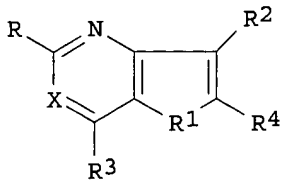
REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L49 ANSWER 26 OF 31 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:511159 CAPLUS
DOCUMENT NUMBER: 131:157709
TITLE: Preparation of bicyclic pyridine and pyrimidine derivatives as neuropeptide Y receptor antagonists
INVENTOR(S): Norman, Mark H.; Chen, Ning; Han, Nianhe; Liu, Longbin; Hurt, Clarence R.; Fotsch, Christopher H.; Jenkins, Tracy J.; Moreno, Ofir A.
PATENT ASSIGNEE(S): Amgen Inc., USA
SOURCE: PCT Int. Appl., 469 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9940091	A1	19990812	WO 1999-US2500	19990205
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6187777	B1	20010213	US 1999-246775	19990204
CA 2319275	AA	19990812	CA 1999-2319275	19990205
EP 1054887	A1	20001129	EP 1999-906756	19990205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 747920	B2	20020530	AU 1999-26590	19990205
AU 9926590	A1	19990823		
JP 2003502272	T2	20030121	JP 2000-530520	19990205
ZA 9900967	A	19990806	ZA 1999-967	19990208

PRIORITY APPLN. INFO.:	US 1998-73927P	P	19980206
	US 1998-73981P	P	19980206
	US 1998-93482P	P	19980720
	US 1998-93577P	P	19980720
	US 1999-246775	A	19990204
	US 1998-83577	P	19980720
	WO 1999-US2500	W	19990205

OTHER SOURCE(S): MARPAT 131:157709
GI



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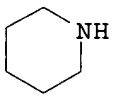
AB Title compds.[I; R = H, CH3, (CH3)2CH, SCH3, CH3CH2, NH2, CF3, NHCOC6H5, cyclopropyl, CH2OH, (CH3)2CH2CH2, N(CH3)2, OCH3, NHCH3, NH(CH2)4NH2; R1 = NH, S, NCH3, O; R2 = H, COCH3, C6H5, CH3, CH3CH2; R3 = NH2, CH3, NHC6H5, N(CH2CH3)2, (CH3CH2)N(CH2)3CH3, (CH3)N(CH2)2NHCH3, N(CH3)CH(CH3)CH(Ph)OH, (CH3CH2)NCH2C(CH3):CH2, NHCH2CF3, NHCH2CH2C6H5, NH(CH2)3OCH2CH3, 4-ClC6H4, 4-CH3OC6H5, 2-thienyl, 1-pyrrolidinyl, 1-piperidinyl, 4-morpholinyl, 1-piperazinyl, 3-pyridyl; R4 = C6H5, 4-CH3C6H4, 4-ClC6H4, (CH3)3C, 4-FC6H4, 3-HOC6H4, 2-pyridyl, cyclohexyl, 2-furyl, 2-FC6H4 2-thienyl, 1-adamantyl, CH3, 4-CH3OC6H4; X = N, CH; etc.], **pharmaceutical** acceptable salts, ester, solvate, and N-oxide are prepd. and tested as neuropeptide Y receptor antagonists in the modulation of feeding behavior, obesity, diabetes, cancer, inflammatory disorders, **depression**, stress related disorders, Alzheimer's disease and other disease conditions. Thus, the title compd. I (R = CH3; R1 = NH; X = N; R2 = H; R3 = N(CH2CH3)2; R4 = C6H5) was prepd.

IT **110-89-4**, Piperidine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of pyrrolopyridine and pyrrolopyrimidine derivs. as neuropeptide Y receptor antagonists)

RN 110-89-4 CAPLUS

CN Piperidine (7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L49 ANSWER 27 OF 31 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:485046 CAPLUS

DOCUMENT NUMBER: 129:109098

TITLE: Preparation and formulation of fused pyrimidine compounds as corticotropin-releasing factor (CRF) receptor antagonists

INVENTOR(S): Tanaka, Hiroshi; Seio, Koji; Kimura, Koreichi; Minoguchi, Masanori; Uehata, Masayoshi; Kohara, Toshiyuki; Ohashi, Yoshitaka; Morio, Yasunori; Yamagami, Keiji

PATENT ASSIGNEE(S): Yoshitomi Pharmaceutical Industries, Ltd., Japan

SOURCE: PCT Int. Appl., 138 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

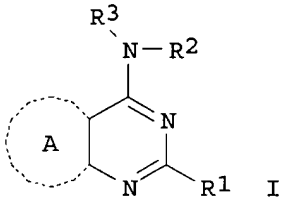
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9829397 A1 19980709 WO 1997-JP4782 19971222
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
AU 9878905 A1 19980731 AU 1998-78905 19971222
PRIORITY APPLN. INFO.: JP 1996-349237 19961227
JP 1997-72410 19970325
WO 1997-JP4782 19971222
OTHER SOURCE(S): MARPAT 129:109098
GI

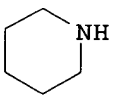


I

AB The title compds. I [ring A = arylphenyl moiety (generic structure given), phenylindole moiety (generic structure given), etc. (said moiety is fused to pyrimidine ring); when ring A is arylphenyl moiety, R1 = H, alkyl, etc., R2, R3 = H, alkyl, aryl, etc.; when ring A is phenylindole , R1 = H, alkyl, cycloalkyl, aryl, etc., R2, R3 = alkyl, cycloalkyl, etc., or NR2R3 = ring] are prepd. I are useful as **drugs**, in particular, remedies for human **depression**, eating disturbance including dietary negativism and overeating, Alzheimer's disease, schizophrenia, Parkinson's disease, Huntington's chorea, amyotrophic lateral sclerosis, mania, psychophysiol. disorder, senile dementia, panic disorder, cerebral attack, inflammation in autoimmune diseases such as rheumatoid arthritis, pain, obesity, Gilles de la Tourette's disease, alc. dependence, climacteric disturbance and premenstrual tension syndrome, cardiac circulatory **drugs** such as hypotensive **drugs**, immunopotentiators, immunosuppressors and **drugs** for improving the conditions of patients in intensive care units (ICU). In in vitro tests for corticotropin-releasing factor (CRF) receptor antagonism, compds. of this invention showed IC50 of < 500 nM.

IT **110-89-4**, Piperidine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of fused pyrimidine compds. as corticotropin-releasing factor (CRF) receptor antagonists)

RN 110-89-4 CAPLUS
CN Piperidine (7CI, 8CI, 9CI) (CA INDEX NAME)



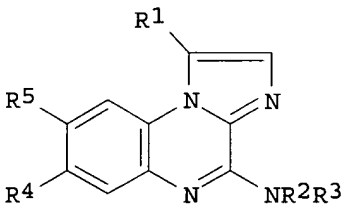
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L49 ANSWER 28 OF 31 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:448087 CAPLUS

DOCUMENT NUMBER: 127:65790
TITLE: Imidazo[1,2-a]quinoxalin-4-amines active as adenosine antagonists, process for their preparation and **pharmaceutical** compositions thereof
INVENTOR(S): Ceccarelli, Stefano; Zanarella, Sergio; Altobelli, Maria; D'Alessandro, Alessandra
PATENT ASSIGNEE(S): Biomedica Foscama Industria Chimico-Farmaceutica S.P.A., Italy; Ceccarelli, Stefano; Zanarella, Sergio; Altobelli, Maria; D'Alessandro, Alessandra
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9719079	A1	19970529	WO 1996-IB1291	19961122
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 865442	A1	19980923	EP 1996-937458	19961122
EP 865442	B1	20000705		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE				
AT 194347	E	20000715	AT 1996-937458	19961122
ES 2149504	T3	20001101	ES 1996-937458	19961122
US 6124287	A	20000926	US 1998-68515	19980512

PRIORITY APPLN. INFO.: IT 1995-MI2446 A 19951124
WO 1996-IB1291 W 19961122
OTHER SOURCE(S): MARPAT 127:65790
GI



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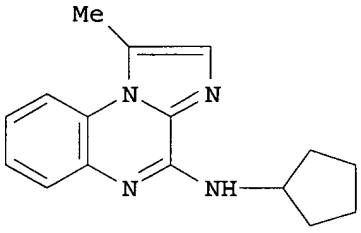
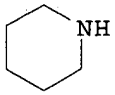


II

AB Imidazo[1,2-a]quinoxalin-4-amines derivs. I [R1 = H, Me; R2 = H, alkyl; R3 = H, alkyl, hydroxyalkyl, cycloalkyl; or R2R3 = (CH2)mZ(CH2)n; Z = bond, O, alkylimino; m, n = 1-3; R4, R5 = H, Cl, F, Br] and salts thereof are described. The compds. are active as adenosine antagonists, and are thus useful for psychiatric and neurol. disorders of the central nervous system, esp. **depression**. For instance, condensation of 1-methylimidazo[1,2-a]quinoxalin-4(5H)-one with cyclopentylamine in hexamethyldisilazane in the presence of (NH4)2SO4 at 120.degree., under Dean-Stark conditions, gave title compd. II. In the mouse tail suspension test, a model for screening of antidepressant activity, II at 0.1 mg/kg i.p. gave a -64.3% variation in immobility time, vs. control. In contrast, desipramine at 16 mg/kg i.p. gave a -62.4% variation in immobility time.

IT **110-89-4**, Piperidine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; prepn. of imidazoquinoxalinamines as adenosine antagonists)
RN 110-89-4 CAPLUS
CN Piperidine (7CI, 8CI, 9CI) (CA INDEX NAME)

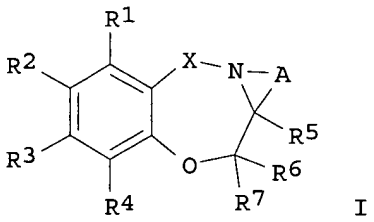

NH

L49 ANSWER 1 OF 31 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:964361 CAPLUS
DOCUMENT NUMBER: 138:24740
TITLE: Preparation of pyrrolo- and pyridobenzoxazepinones and related compounds as AMPA receptor agonists
INVENTOR(S): Grove, Simon James Anthony; Zhang, Mingqiang; Shahid, Mohammad
PATENT ASSIGNEE(S): Akzo Nobel N.V., Neth.
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002100865	A1	20021219	WO 2002-EP6185	20020605

W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EC, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, RO, RU, SG, SI, SK, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2001-202215 A 20010611
OTHER SOURCE(S): MARPAT 138:24740
GI

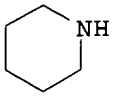


I

AB Title compds. [I; X = CO , SO2; R1-R4 = H, alkyl, alkyloxy, alkyloxyalkyl, halo, NO2, cyano, NR8R9, NR8COR10, CONR8R9; R5-R7 = H, alkyl; R8, R9 = H, alkyl; R8R9N = 5-6 membered satd. heterocyclic ring, optionally contg. O, S, NR11; R10, R11 = alkyl; A = residue of a 4-7 membered satd. heterocyclic ring optionally contg. an O atom, optionally substituted with 1-3 alkyl, alkoxy, OH, halo, oxo; with provisos], were prepd. Thus, 2,5-difluorobenzoic acid in DMF was treated with 1,1'-carbonyldiimidazole and the soln. stirred at room temp. for 1 h, followed by the addn. of (R)-(-)-2-pyrrolidinemethanol; the mixt. was stirred at room temp. overnight whereupon NaH in mineral oil was added and the mixt. was heated to 120.degree. for 2 h to give (R)-7-fluoro-2,3,11,11a-tetrahydro-1H,5H-pyrrolo[2,1-c][1,4]benzoxazepine-5-one. The latter at 10 .mu.M gave a 17% increase in glutamate-evoked steady state current from postnatal hippocampal neurons.

IT **110-89-4**, Piperidine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of pyrrolo- and pyridobenzoxazepinones and related compds. as AMPA receptor agonists)

RN 110-89-4 CAPLUS
CN Piperidine (7CI, 8CI, 9CI) (CA INDEX NAME)



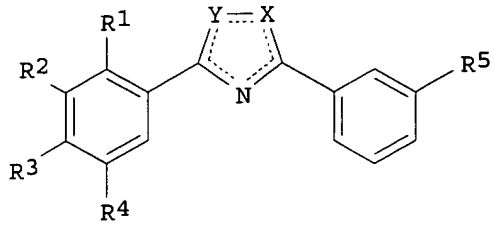
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitstr 20-31

L49 ANSWER 20 OF 31 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:62381 CAPLUS
DOCUMENT NUMBER: 134:115960
TITLE: Triazole and imidazole derivatives, methods of preparation and use in treatment or prophylaxis of diseases caused by overactivation of respective NMDA receptor subtypes
INVENTOR(S): Alanine, Alexander; Buettelmann, Bernd; Heitz, Neidhart Marie-Paule; Jaeschke, Georg; Pinard, Emmanuel; Wyler, Rene
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: Eur. Pat. Appl., 66 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1070708	A1	20010124	EP 2000-114183	20000713
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6265426	B1	20010724	US 2000-619518	20000719
NO 2000003723	A	20010122	NO 2000-3723	20000720
ZA 2000003680	A	20010122	ZA 2000-3680	20000720
CN 1281852	A	20010131	CN 2000-120181	20000720
BR 2000003075	A	20010313	BR 2000-3075	20000721
JP 2001064263	A2	20010313	JP 2000-220748	20000721

PRIORITY APPLN. INFO.: EP 1999-114313 A 19990721
OTHER SOURCE(S): MARPAT 134:115960
GI



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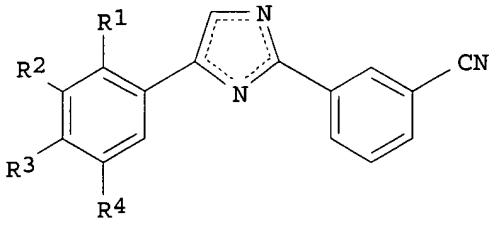


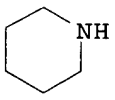
II

AB The present invention relates to I wherein R1-R4 = H, CF3, OCF3, OCHF2, OCH2F, lower alkyl, lower alkoxy, halogen, hydroxy, Ph, benzyl, amino, nitro, pyrrol-1-yl, lower alkylsulfonyl, lower alkylthio, cyano or benzyloxy; or R2 and R3 may be together = O-(CH2)2-O-, -O-CH2-O-, -O-(CH2)2-, -(CH2)3- or CH:CH-CH:CH-; X = N:, imino with N possibly substituted, CH:; Y = -N:, :N-, imino with N possibly substituted, CH:; wherein one of X or Y has to be N; R5 = aminomethyl with N possibly substituted and to their **pharmaceutically** acceptable acid addn. salts. The methods of prepn. comprise cyclizing a carboxylic acid hydrazide with a benzenecarboximidamide hydrochloride or benzenecarboximidic acid ester to give a triazole; arylating a 4-iodo-2-phenylimidazole with a phenylboronic acid in the presence of Pd(PPh3)4 to give an imidazole; reducing II to the aminomethyl analog followed by di-N-alkylation using acyl chlorides and LiAlH4. These compds. may be used for the treatment or prophylaxis of diseases related to the N-methyl-D-aspartate (NMDA)-receptor-subtype selective blockers. Such diseases include acute forms of neurodegeneration caused, e.g., by stroke or brain trauma; chronic forms of neurodegeneration such as Alzheimer's disease, Parkinson's disease, Huntington's disease or ALS (amyotrophic lateral sclerosis); neurodegeneration assocd. with bacterial or viral infections, and diseases such as schizophrenia, anxiety, **depression** and acute/chronic pain.

IT **110-89-4**, Piperidine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(triazole and imidazole derivs., methods of prepn. and use in treatment or prophylaxis of diseases caused by overactivation of resp. NMDA receptor subtypes)

RN 110-89-4 CAPLUS

CN Piperidine (7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L49 ANSWER 21 OF 31 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:861662 CAPLUS
DOCUMENT NUMBER: 134:29325
TITLE: Preparation of metabotropic glutamate receptor

antagonists and their use for treating central nervous system diseases

INVENTOR(S): Van Wagenen, Bradford C.; Moe, Scott T.; Smith, Daryl L.; Sheehan, Susan M.; Shcherbakova, Irina; Travato, Richard; Walton, Ruth; Barmore, Robert; Delmar, Eric G.; Stormann, Thomas M.

PATENT ASSIGNEE(S): NPS Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000073283	A1	20001207	WO 2000-US15222	20000602
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1196397	A1	20020417	EP 2000-936465	20000602
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003500480	T2	20030107	JP 2000-621349	20000602

PRIORITY APPLN. INFO.: US 1999-137272P P 19990602
WO 2000-US15222 W 20000602

OTHER SOURCE(S): MARPAT 134:29325

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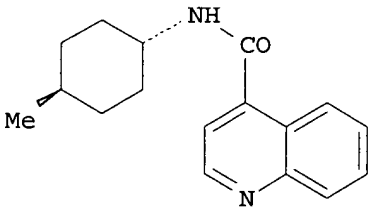
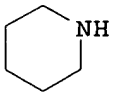


I

AB Title compds. [R1NHCOR; R = quinolinyl, quinoxalinyl, thiazolidinyl, Ph, benzimidazoyl, pyridyl, naphthyridinyl; R1 = phenylpropyl, cyclopentyl, pentyl, cyclohexyl, quinolinyl], stereoisomers, and **pharmaceutically** acceptable salts are prepd. and are active as metabotropic glutamate receptor antagonists (no data). Title compds. are useful for treating neurol. diseases and disorders in **pharmaceutical** compns. Thus, the title compd. I was prepd. for treating disease assocd. with glutamate-induced neuronal damage.

IT **110-89-4**, Piperidine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of mGluR antagonists for treating central nervous system diseases)

RN 110-89-4 CAPLUS
CN Piperidine (7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L49 ANSWER 22 OF 31 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:861658 CAPLUS
DOCUMENT NUMBER: 134:29425
TITLE: Novel 4-phenyl-pyrimidine derivatives as NK-1 receptor antagonists
INVENTOR(S): Boes, Michael; Galley, Guido; Godel, Thierry; Hoffmann, Torsten; Hunkeler, Walter; Schnider, Patrick; Stadler, Heinz
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000073279	A1	20001207	WO 2000-EP4701	20000524
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6274588	B1	20010814	US 2000-575382	20000522
BR 2000011127	A	20020219	BR 2000-11127	20000524
EP 1187815	A1	20020320	EP 2000-927234	20000524
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003500478	T2	20030107	JP 2000-621345	20000524
NO 2001005700	A	20011122	NO 2001-5700	20011122

PRIORITY APPLN. INFO.: EP 1999-110483 A 19990531
WO 2000-EP4701 W 20000524

OTHER SOURCE(S): MARPAT 134:29425
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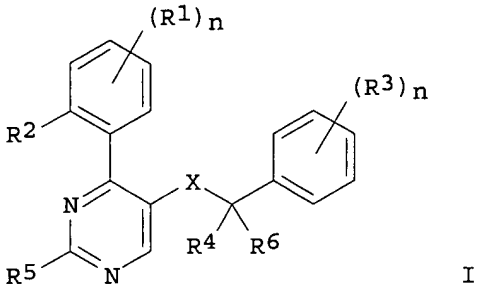

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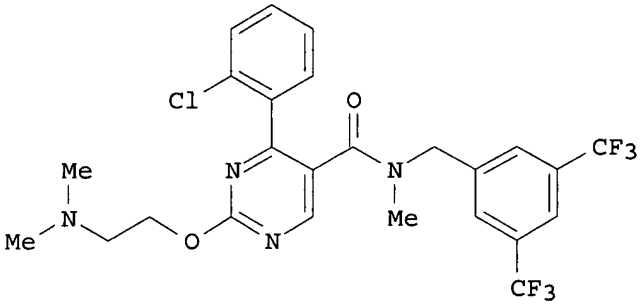


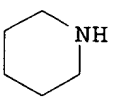
II

AB The invention discloses pyrimidine derivs. I [R1 = H or halo; R2 = H, halo, lower alkyl or lower alkoxy; R1 and R2 may be together with the two carbon atoms -CH=CH-CH=CH-; R3 = halo, CF3, lower alkyl or lower alkoxy; R4, R6 = (independently) H or lower alkyl; R5 = lower alkyl, lower alkoxy, amino, Ph, hydroxy-lower alkyl, cyano-lower alkyl, carbamoyl-lower alkyl, pyridyl, pyrimidyl, (un)substituted -(CH2)n-piperazinyl, which is optionally substituted by one or two lower alkyl groups or by hydroxy-lower alkyl, -(CH2)n-morpholinyl, -(CH2)n-piperidinyl, -(CH2)n+1-imidazolyl, lower alkyl-sulfanyl, lower alkyl-sulfonyl, benzylamino, -NH-(CH2)n+1N(R7)2, -(CH2)n+1N(R7)2, -O-(CH2)n+1-morpholinyl, -O-(CH2)n+1-piperidinyl or -O-(CH2)n+1N(R7)2, wherein R7 = H or lower alkyl; n = 0-2; X = -C(O)N(R7)- or -N(R7)C(O)-] and their **pharmaceutically** acceptable acid addn. salts as NK-1 receptor antagonists. The preferred compds. exhibited pKi values for NK-1 receptor affinity in the range of 8.00-9.20, e.g., the pKi of II was 8.45. With demonstrated affinity to the NK-1 receptor, these compds. may prove useful for the treatment of medical conditions related to this receptor, e.g., inflammatory conditions such as arthritis, migraine, asthma, etc., and in particular CNS disorders such as **depression** or emesis.

IT **110-89-4**, Piperidine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn and biol. activity of phenylpyrimidine derivs. as NK-1 antagonists)

RN 110-89-4 CAPLUS

CN Piperidine (7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L49 ANSWER 23 OF 31 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:772614 CAPLUS
DOCUMENT NUMBER: 133:335165
TITLE: 2-Aminoquinolinecarboxamides: neurokinin receptor ligands
INVENTOR(S): Yuan, Jun; Maynard, George; Hutchison, Alan
PATENT ASSIGNEE(S): Neurogen Corporation, USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000064877	A1	20001102	WO 2000-US11187	20000426
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6369053	B1	20020409	US 2000-560160	20000428
US 2002156095	A1	20021024	US 2002-115409	20020403

PRIORITY APPLN. INFO.: US 1999-131025P P 19990426
US 2000-560160 A1 20000428
OTHER SOURCE(S): MARPAT 133:335165
GI

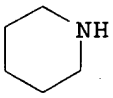
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. I (X = O, S or N-CN; R1 = H, halo, OH, NO2, CN, SO2NH2, C1-6alkyl, OC1-6alkyl, SO2NHC1-6alkyl, N(C1-6alkyl)2, etc. where C1-6alkyl may be (un)substituted, branched, cyclic, or unsatd.; R2 or R3 = H, halo, OH, NO2, CN, SO2NH2, (un)substituted aryl [aryl may be Ph, naphthyl, thienyl, etc.], C1-8alkyl, OC1-8alkyl, SO2NHC1-8alkyl, N(C1-8alkyl)2, etc. where C1-8alkyl may be (un)substituted, branched, cyclic, or unsatd.; R4 or R5 = independently Q1 or Q2 where R7 = H or C1-8alkyl as defined above and R8 or R9 = H, C1-8alkyl as defined above, aldehyde, ketone, amide, sulfonamide, (un)substituted aryl [aryl may be Ph, naphthyl, thienyl, etc.] or R8R9 join to form a 4-8 membered monocyclic or bicyclic ring [which may contain unsaturations, heteroatoms or R1]) and their **pharmaceutically** acceptable salts or **pharmaceutically** acceptable solvates thereof are disclosed as neurokinin receptor ligands. Thus, compd. II was prepd. by substitution of the corresponding 2-bromo quinoline deriv. with pyrrolidine. As ligands of neurokinin receptors, in particular NK-3 receptors, the compds. disclosed (no data) are useful in the treatment of a wide range of diseases or disorders including, but not limited to **depression**, anxiety, psychosis, obesity, pain, Parkinson's disease, Alzheimer's disease, neurodegenerative diseases, movement disorders, respiratory diseases, inflammatory diseases, neuropathy, immune disorders, migraine, biliary disfunction, and dermatitis.

IT **110-89-4**, Piperidine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn of aminoquinolinecarboxamides as neurokinin receptor antagonists)

RN 110-89-4 CAPLUS

CN Piperidine (7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L49 ANSWER 24 OF 31 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:688232 CAPLUS
DOCUMENT NUMBER: 133:266729
TITLE: Preparation of novel substituted tetrahydropyrans as neurokinin 1 (NK-1) receptor antagonists
INVENTOR(S): Owen, Simon Neil; Seward, Eileen Mary; Swain, Christopher John; Williams, Brian John
PATENT ASSIGNEE(S): Merck Sharp & Dohme Limited, UK
SOURCE: PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000056727	A1	20000928	WO 2000-GB974	20000316
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1165540	A1	20020102	EP 2000-911045	20000316
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 746251	B2	20020418	AU 2000-33042	20000316
JP 2002540107	T2	20021126	JP 2000-606588	20000316
US 6458830	B1	20021001	US 2001-936343	20010910

PRIORITY APPLN. INFO.:
GB 1999-6480 A 19990319
GB 1999-24616 A 19991018
WO 2000-GB974 W 20000316

OTHER SOURCE(S): MARPAT 133:266729
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

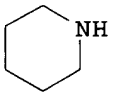
AB Substituted tetrahydropyrans I [R1, R4 = H, halo, alkyl, alkoxy, fluoroalkyl, fluoroalkoxy, cycloalkyl(alkyl), NO2, CN, SRa, SORa, SO2Ra, CO2Ra, CONRaRb (Ra or Rb = H, alkyl), alkenyl, alkynyl, alkoxy(alkyl); R2, R5 = H, halo, alkyl, fluoroalkyl, alkoxyalkoxy; R3 = H, halo, fluoroalkyl; R6 = H, alkyl, hydroxyalkyl; R7 = halo, hydroxy, (un)substituted alkenyl, (un)substituted alkynyl, N3, -NR11R12, -NRaCORb, -OSO2Ra, -(CH2)pNRa(CH2)qCOORb (p or q = 1, 2), CORa, COORa, -N=C=O, or N/O/S heterocycle bound at N optionally substituted by oxo, thioxo, halogen,

hydroxy, thiol, CORa, CO2Ra, -ZNR11R12 (Z = bond, cyclo(alkylene)), alkyl, hydroxyalkyl, haloalkyl, alkoxy, fluoroalkoxy or alkoxy substituted by a alkoxy or hydroxyl group (R11 = H, alkyl, cycloalkyl, cycloalkylalkyl, alkyl substituted by alkoxy or hydroxyl group, five or six membered N heterocycle; R12 = H, alkyl, cycloalkyl, cycloalkylalkyl, alkyl substituted by alkoxy or hydroxyl group); R8 = hydrogen, alkyl, fluoroalkyl, hydroxy, alkoxy, hydroxyalkyl; R9 or R10 = H, halo, alkyl, oxo, CO2Ra, CONRaRb, CH2ORc (Rc = H, alkyl, phenyl); n = 0, 1 or 2] and **pharmaceutically** acceptable salts thereof were prepd. as neurokinin 1 (NK-1) receptor antagonists. Thus, tetrahydropyran II (R = Me2N) was prepd. via nucleophilic substitution of the corresponding mesylate II (R = MeSO2O). The compds. are of particular use in the treatment or prevention of **depression**, anxiety, pain, inflammation, migraine, emesis or postherpetic neuralgia (no data).

IT **110-89-4**, Piperidine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of substituted tetrahydropyrans as neurokinin 1 (NK-1) receptor antagonists)

RN 110-89-4 CAPLUS

CN Piperidine (7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L49 ANSWER 25 OF 31 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:412296 CAPLUS

DOCUMENT NUMBER: 133:115233

TITLE: Recent advances in neurokinin-3 receptor antagonists

AUTHOR(S): Giardina, Giuseppe A. M.; Grugni, Mario; Raveglia, Luca F.

CORPORATE SOURCE: Department of Medicinal Chemistry, SmithKline Beecham SpA, Milan, 20021, Italy

SOURCE: Expert Opinion on Therapeutic Patents (2000), 10(6), 939-960
CODEN: EOTPEG; ISSN: 1354-3776

PUBLISHER: Ashley Publications Ltd.

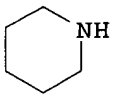
DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review, with 117 refs., of recent highlights and progress made in the neurokinin-3 (NK-3) receptor area since 1997. Whereas in the neurokinin-1 (NK-1) and neurokinin-2 (NK-2) biol. areas literature information based on clin. data account for a high therapeutic potential (in emesis and **depression** for NK-1 and asthma for NK-2 receptor antagonists), there is a total deficiency of information from NK-3 receptor antagonists in clin. development. No other chem. classes in addn. to dichlorophenylalkylpiperidines, represented by SR 142,801 and quinolines, represented by SB-222200 and SB-223412, have been identified by **pharmaceutical** companies and scientists involved in the specific field. Biol. evidence indicates pain/inflammation as a suitable CNS-related therapeutic target, this conclusion is based on localization studies and efficacy of selected NK-3 receptor antagonists in rat disease models of inflammatory pain. In the periphery, the most likely therapeutic indications might be pulmonary and gastrointestinal tract diseases. It is clearly still premature to anticipate any therapeutic potential in man.

IT **110-89-4D**, Piperidine, dichlorophenylalkyl derivs., biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neurokinin-3 receptor antagonists therapeutic potential)
RN 110-89-4 CAPLUS
CN Piperidine (7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L49 ANSWER 26 OF 31 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:511159 CAPLUS
DOCUMENT NUMBER: 131:157709
TITLE: Preparation of bicyclic pyridine and pyrimidine derivatives as neuropeptide Y receptor antagonists
INVENTOR(S): Norman, Mark H.; Chen, Ning; Han, Nianhe; Liu, Longbin; Hurt, Clarence R.; Fotsch, Christopher H.; Jenkins, Tracy J.; Moreno, Ofir A.
PATENT ASSIGNEE(S): Amgen Inc., USA
SOURCE: PCT Int. Appl., 469 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9940091	A1	19990812	WO 1999-US2500	19990205
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6187777	B1	20010213	US 1999-246775	19990204
CA 2319275	AA	19990812	CA 1999-2319275	19990205
EP 1054887	A1	20001129	EP 1999-906756	19990205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 747920	B2	20020530	AU 1999-26590	19990205
AU 9926590	A1	19990823		
JP 2003502272	T2	20030121	JP 2000-530520	19990205
ZA 9900967	A	19990806	ZA 1999-967	19990208

PRIORITY APPLN. INFO.:
US 1998-73927P P 19980206
US 1998-73981P P 19980206
US 1998-93482P P 19980720
US 1998-93577P P 19980720
US 1999-246775 A 19990204
US 1998-83577 P 19980720
WO 1999-US2500 W 19990205

OTHER SOURCE(S): MARPAT 131:157709
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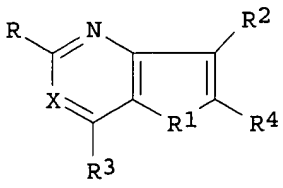


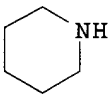
I

AB Title compds.[I; R = H, CH3, (CH3)2CH, SCH3, CH3CH2, NH2, CF3, NHCOC6H5, cyclopropyl, CH2OH, (CH3)2CH2CH2, N(CH3)2, OCH3, NHCH3, NH(CH2)4NH2; R1 = NH, S, NCH3, O; R2 = H, COCH3, C6H5, CH3, CH3CH2; R3 = NH2, CH3, NHC6H5, N(CH2CH3)2, (CH3CH2)N(CH2)3CH3, (CH3)N(CH2)2NHCH3, N(CH3)CH(CH3)CH(Ph)OH, (CH3CH2)NCH2C(CH3):CH2, NHCH2CF3, NHCH2CH2C6H5, NH(CH2)3OCH2CH3, 4-ClC6H4, 4-CH3OC6H5, 2-thienyl, 1-pyrrolidinyl, 1-piperidinyl, 4-morpholinyl, 1-piperazinyl, 3-pyridyl; R4 = C6H5, 4-CH3C6H4, 4-ClC6H4, (CH3)3C, 4-FC6H4, 3-HOC6H4, 2-pyridyl, cyclohexyl, 2-furyl, 2-FC6H4 2-thienyl, 1-adamantyl, CH3, 4-CH3OC6H4; X = N, CH; etc.], **pharmaceutical** acceptable salts, ester, solvate, and N-oxide are prepd. and tested as neuropeptide Y receptor antagonists in the modulation of feeding behavior, obesity, diabetes, cancer, inflammatory disorders, **depression**, stress related disorders, Alzheimer's disease and other disease conditions. Thus, the title compd. I (R = CH3; R1 = NH; X = N; R2 = H; R3 = N(CH2CH3)2; R4 = C6H5) was prepd.

IT **110-89-4**, Piperidine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of pyrrolopyridine and pyrrolopyrimidine derivs. as neuropeptide Y receptor antagonists)

RN 110-89-4 CAPLUS

CN Piperidine (7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L49 ANSWER 27 OF 31 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:485046 CAPLUS

DOCUMENT NUMBER: 129:109098

TITLE: Preparation and formulation of fused pyrimidine compounds as corticotropin-releasing factor (CRF) receptor antagonists

INVENTOR(S): Tanaka, Hiroshi; Seio, Koji; Kimura, Koreichi; Minoguchi, Masanori; Uehata, Masayoshi; Kohara, Toshiyuki; Ohashi, Yoshitaka; Morio, Yasunori; Yamagami, Keiji

PATENT ASSIGNEE(S): Yoshitomi Pharmaceutical Industries, Ltd., Japan

SOURCE: PCT Int. Appl., 138 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

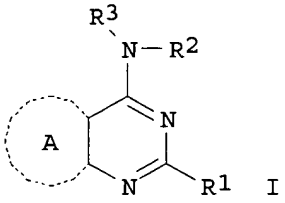
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9829397 A1 19980709 WO 1997-JP4782 19971222
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
AU 9878905 A1 19980731 AU 1998-78905 19971222
PRIORITY APPLN. INFO.: JP 1996-349237 19961227
JP 1997-72410 19970325
WO 1997-JP4782 19971222
OTHER SOURCE(S): MARPAT 129:109098
GI

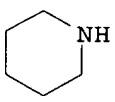


I

AB The title compds. I [ring A = arylphenyl moiety (generic structure given), phenylindole moiety (generic structure given), etc. (said moiety is fused to pyrimidine ring); when ring A is arylphenyl moiety, R1 = H, alkyl, etc., R2, R3 = H, alkyl, aryl, etc.; when ring A is phenylindole , R1 = H, alkyl, cycloalkyl, aryl, etc., R2, R3 = alkyl, cycloalkyl, etc., or NR2R3 = ring] are prepd. I are useful as **drugs**, in particular, remedies for human **depression**, eating disturbance including dietary negativism and overeating, Alzheimer's disease, schizophrenia, Parkinson's disease, Huntington's chorea, amyotrophic lateral sclerosis, mania, psychophysiol. disorder, senile dementia, panic disorder, cerebral attack, inflammation in autoimmune diseases such as rheumatoid arthritis, pain, obesity, Gilles de la Tourette's disease, alc. dependence, climacteric disturbance and premenstrual tension syndrome, cardiac circulatory **drugs** such as hypotensive **drugs**, immunopotentiators, immunosuppressors and **drugs** for improving the conditions of patients in intensive care units (ICU). In in vitro tests for corticotropin-releasing factor (CRF) receptor antagonism, compds. of this invention showed IC50 of < 500 nM.

IT **110-89-4**, Piperidine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of fused pyrimidine compds. as corticotropin-releasing factor (CRF) receptor antagonists)

RN 110-89-4 CAPLUS
CN Piperidine (7CI, 8CI, 9CI) (CA INDEX NAME)



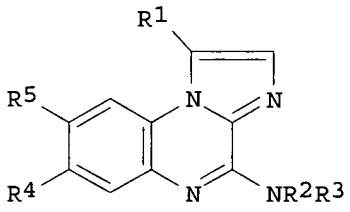
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L49 ANSWER 28 OF 31 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:448087 CAPLUS

DOCUMENT NUMBER: 127:65790
TITLE: Imidazo[1,2-a]quinoxalin-4-amines active as adenosine antagonists, process for their preparation and **pharmaceutical** compositions thereof
INVENTOR(S): Ceccarelli, Stefano; Zanarella, Sergio; Altobelli, Maria; D'Alessandro, Alessandra
PATENT ASSIGNEE(S): Biomedica Foscama Industria Chimico-Farmaceutica S.P.A., Italy; Ceccarelli, Stefano; Zanarella, Sergio; Altobelli, Maria; D'Alessandro, Alessandra
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9719079	A1	19970529	WO 1996-IB1291	19961122
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 865442	A1	19980923	EP 1996-937458	19961122
EP 865442	B1	20000705		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE				
AT 194347	E	20000715	AT 1996-937458	19961122
ES 2149504	T3	20001101	ES 1996-937458	19961122
US 6124287	A	20000926	US 1998-68515	19980512

PRIORITY APPLN. INFO.: IT 1995-MI2446 A 19951124
WO 1996-IB1291 W 19961122
OTHER SOURCE(S): MARPAT 127:65790
GI



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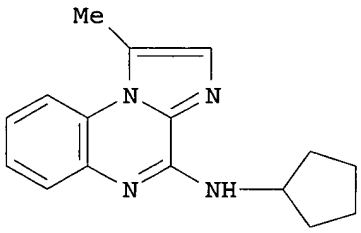
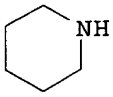


II

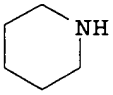
AB Imidazo[1,2-a]quinoxalin-4-amines derivs. I [R1 = H, Me; R2 = H, alkyl; R3 = H, alkyl, hydroxyalkyl, cycloalkyl; or R2R3 = (CH2)mZ(CH2)n; Z = bond, O, alkylimino; m, n = 1-3; R4, R5 = H, Cl, F, Br] and salts thereof are described. The compds. are active as adenosine antagonists, and are thus useful for psychiatric and neurol. disorders of the central nervous system, esp. **depression**. For instance, condensation of 1-methylimidazo[1,2-a]quinoxalin-4(5H)-one with cyclopentylamine in hexamethyldisilazane in the presence of (NH4)2SO4 at 120.degree., under Dean-Stark conditions, gave title compd. II. In the mouse tail suspension test, a model for screening of antidepressant activity, II at 0.1 mg/kg i.p. gave a -64.3% variation in immobility time, vs. control. In contrast, desipramine at 16 mg/kg i.p. gave a -62.4% variation in immobility time.

IT **110-89-4**, Piperidine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; prepn. of imidazoquinoxalinamines as adenosine antagonists)

RN 110-89-4 CAPLUS
CN Piperidine (7CI, 8CI, 9CI) (CA INDEX NAME)



CN Piperidine (7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L49 ANSWER 24 OF 31 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:688232 CAPLUS
DOCUMENT NUMBER: 133:266729
TITLE: Preparation of novel substituted tetrahydropyrans as neurokinin 1 (NK-1) receptor antagonists
INVENTOR(S): Owen, Simon Neil; Seward, Eileen Mary; Swain, Christopher John; Williams, Brian John
PATENT ASSIGNEE(S): Merck Sharp & Dohme Limited, UK
SOURCE: PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000056727	A1	20000928	WO 2000-GB974	20000316
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1165540	A1	20020102	EP 2000-911045	20000316
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 746251	B2	20020418	AU 2000-33042	20000316
JP 2002540107	T2	20021126	JP 2000-606588	20000316
US 6458830	B1	20021001	US 2001-936343	20010910

PRIORITY APPLN. INFO.: GB 1999-6480 A 19990319
GB 1999-24616 A 19991018
WO 2000-GB974 W 20000316
OTHER SOURCE(S): MARPAT 133:266729
GI

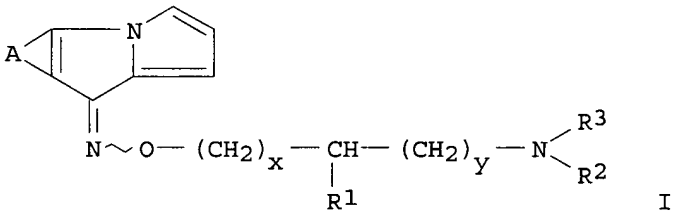
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Substituted tetrahydropyrans I [R1, R4 = H, halo, alkyl, alkoxy, fluoroalkyl, fluoroalkoxy, cycloalkyl(alkyl), NO2, CN, SRa, SORa, SO2Ra, CO2Ra, CONRaRb (Ra or Rb = H, alkyl), alkenyl, alkynyl, alkoxy(alkyl); R2, R5 = H, halo, alkyl, fluoroalkyl, alkoxyalkoxy; R3 = H, halo, fluoroalkyl; R6 = H, alkyl, hydroxyalkyl; R7 = halo, hydroxy, (un)substituted alkenyl, (un)substituted alkynyl, N3, -NR11R12, -NRaCORb, -OSO2Ra, -(CH2)pNRa(CH2)qCOORb (p or q = 1, 2), CORa, COORa, -N=C=O, or N/O/S heterocycle bound at N optionally substituted by oxo, thioxo, halogen,

L49 ANSWER 30 OF 31 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:485727 CAPLUS
DOCUMENT NUMBER: 125:142700
TITLE: Tricyclic oxime ethers process for their preparation and **pharmaceutical** compositions containing them
INVENTOR(S): Rault, Sylvain; Robba, Max; Lancelot, Jean-Charles; Prunier, Herve; Renard, Pierre; Pfeiffer, Bruno; Guardiola-Lemaitre, Beatrice; Rettori, Marie-Claire
PATENT ASSIGNEE(S): Adir Et Compagnie, Fr.
SOURCE: Eur. Pat. Appl., 45 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 718299	A1	19960626	EP 1995-402865	19951219
EP 718299	B1	20000405		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
FR 2728571	A1	19960628	FR 1994-15431	19941222
FR 2728571	B1	19970131		
CA 2165618	AA	19960623	CA 1995-2165618	19951219
AT 191483	E	20000415	AT 1995-402865	19951219
ES 2147271	T3	20000901	ES 1995-402865	19951219
FI 9506136	A	19960623	FI 1995-6136	19951220
AU 9540593	A1	19960627	AU 1995-40593	19951220
AU 693615	B2	19980702		
NO 9505215	A	19960624	NO 1995-5215	19951221
ZA 9510901	A	19960624	ZA 1995-10901	19951221
JP 08231554	A2	19960910	JP 1995-333347	19951221
JP 2937837	B2	19990823		
US 5627203	A	19970506	US 1995-576678	19951221
CN 1131155	A	19960918	CN 1995-120144	19951222
CN 1066449	B	20010530		
CN 1261073	A	20000726	CN 1999-120993	19991203

PRIORITY APPLN. INFO.: FR 1994-15431 A 19941222
OTHER SOURCE(S): MARPAT 125:142700
GI



I

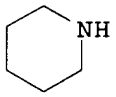
AB The present invention concerns compds. I, in which A represents a thieno group, x and y are independently 0-4, R1 is H, alkyl, alkenyl, cycloalkyl, OH, alkoxy, substituted Ph, phenylalkyl, substituted phenoxy, R2 and R3 are H, alkyl, alkenyl, cycloalkyl, substituted indanyl, substituted Ph, phenylalkyl, or R2 and R3 form azacycloalkyl rings, and their oxalates or fumarates. I, e.g. II (X = NOCHPhCH2CH2NMe2) are prepd. from the ketone, e.g II (X = O), via hydroxyimination followed by O-alkylation, e.g with PhCHClCH2CH2NMe2.cntdot.HCl. I were tested as serotoninergic receptor antagonists (IC50 1.1 x 10 -10 to 10-4 M), anxiolytics and

antidepressants.

IT **110-89-4**, Piperidine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of tricyclic oxime ethers as serotoninergic receptor antagonists)

RN 110-89-4 CAPLUS

CN Piperidine (7CI, 8CI, 9CI) (CA INDEX NAME)



L49 ANSWER 31 OF 31 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1985:170 CAPLUS

DOCUMENT NUMBER: 102:170

TITLE: Synthesis of some substituted benzodiazepines as possible CNS depressant **drugs**

AUTHOR(S): Dhasmana, A.; Mehrotra, S.; Gupta, T. K.; Bhargava, K. P.; Parmar, S. S.; Barthwal, J. P.

CORPORATE SOURCE: Jawahar Lal Nehru Lab. Mol. Biol., King George's Med. Coll., Lucknow, India

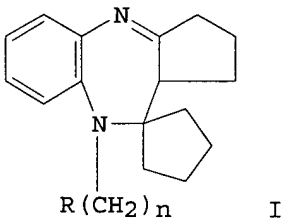
SOURCE: Arzneimittel-Forschung (1984), 34(9), 943-5
CODEN: ARZNAD; ISSN: 0004-4172

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 102:170

GI



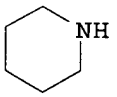
I

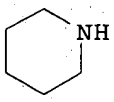
AB A series of 2,3-cyclopentano-3,4-dihydro-4-spirocyclopentano-1,5-benzodiazepines I (where R = pyrrolidine, morpholine, piperidine, or 2-methylpiperidine; n = 2 or 3) were prepd. and evaluated for their central nervous system (CNS) depressant activity in mice. Most of the compds. tested had CNS depressant activity. These compds. were also good inhibitors of succinate dehydrogenase [9002-02-2] in vitro. These compds. showed low toxicity. Structure-activity relations are discussed.

IT **110-89-4**, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with spirocyclopentanobenzodiazepines)

RN 110-89-4 CAPLUS

CN Piperidine (7CI, 8CI, 9CI) (CA INDEX NAME)




NH

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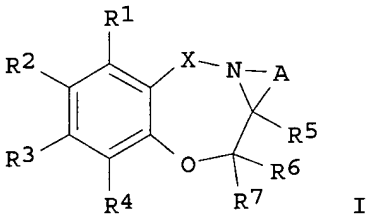
L49 ANSWER 1 OF 31 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:964361 CAPLUS
DOCUMENT NUMBER: 138:24740
TITLE: Preparation of pyrrolo- and pyridobenzoxazepinones and related compounds as AMPA receptor agonists
INVENTOR(S): Grove, Simon James Anthony; Zhang, Mingqiang; Shahid, Mohammad
PATENT ASSIGNEE(S): Akzo Nobel N.V., Neth.
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002100865	A1	20021219	WO 2002-EP6185	20020605

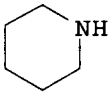
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EC, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, RO, RU, SG, SI, SK, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2001-202215 A 20010611
OTHER SOURCE(S): MARPAT 138:24740
GI



I

AB Title compds. [I; X = CO , SO2; R1-R4 = H, alkyl, alkyloxy, alkyloxyalkyl, halo, NO2, cyano, NR8R9, NR8COR10, CONR8R9; R5-R7 = H, alkyl; R8, R9 = H, alkyl; R8R9N = 5-6 membered satd. heterocyclic ring, optionally contg. O, S, NR11; R10, R11 = alkyl; A = residue of a 4-7 membered satd. heterocyclic ring optionally contg. an O atom, optionally substituted with 1-3 alkyl, alkoxy, OH, halo, oxo; with provisos], were prepd. Thus, 2,5-difluorobenzoic acid in DMF was treated with 1,1'-carbonyldiimidazole and the soln. stirred at room temp. for 1 h, followed by the addn. of (R)-(-)-2-pyrrolidinemethanol; the mixt. was stirred at room temp. overnight whereupon NaH in mineral oil was added and the mixt. was heated to 120.degree. for 2 h to give (R)-7-fluoro-2,3,11,11a-tetrahydro-1H,5H-pyrrolo[2,1-c][1,4]benzoxazepine-5-one. The latter at 10 .mu.M gave a 17% increase in glutamate-evoked steady state current from postnatal hippocampal neurons.
IT **110-89-4**, Piperidine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of pyrrolo- and pyridobenzoxazepinones and related compds. as AMPA receptor agonists)
RN 110-89-4 CAPLUS
CN Piperidine (7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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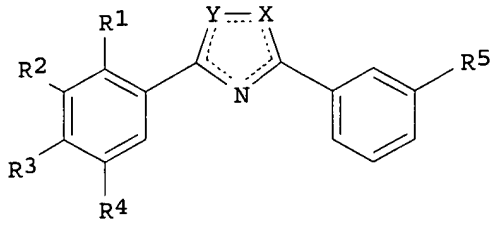
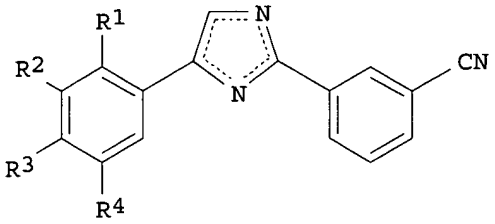
L49 ANSWER 20 OF 31 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:62381 CAPLUS
DOCUMENT NUMBER: 134:115960
TITLE: Triazole and imidazole derivatives, methods of preparation and use in treatment or prophylaxis of diseases caused by overactivation of respective NMDA receptor subtypes
INVENTOR(S): Alanine, Alexander; Buettelmann, Bernd; Heitz, Neidhart Marie-Paule; Jaeschke, Georg; Pinard, Emmanuel; Wyler, Rene
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: Eur. Pat. Appl., 66 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1070708	A1	20010124	EP 2000-114183	20000713
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6265426	B1	20010724	US 2000-619518	20000719
NO 2000003723	A	20010122	NO 2000-3723	20000720
ZA 2000003680	A	20010122	ZA 2000-3680	20000720
CN 1281852	A	20010131	CN 2000-120181	20000720
BR 2000003075	A	20010313	BR 2000-3075	20000721
JP 2001064263	A2	20010313	JP 2000-220748	20000721

PRIORITY APPLN. INFO.: EP 1999-114313 A 19990721
OTHER SOURCE(S): MARPAT 134:115960
GI



I



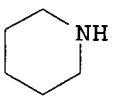
II

AB The present invention relates to I wherein R1-R4 = H, CF3, OCF3, OCHF2, OCH2F, lower alkyl, lower alkoxy, halogen, hydroxy, Ph, benzyl, amino, nitro, pyrrol-1-yl, lower alkylsulfonyl, lower alkylthio, cyano or benzyloxy; or R2 and R3 may be together = O-(CH2)2-O-, -O-CH2-O-, -O-(CH2)2-, -(CH2)3- or CH:CH-CH:CH-; X = N:, imino with N possibly substituted, CH:; Y = -N:, :N-, imino with N possibly substituted, CH:; wherein one of X or Y has to be N; R5 = aminomethyl with N possibly substituted and to their **pharmaceutically** acceptable acid addn. salts. The methods of prepn. comprise cyclizing a carboxylic acid hydrazide with a benzenecarboximidamide hydrochloride or benzenecarboximidic acid ester to give a triazole; arylating a 4-iodo-2-phenylimidazole with a phenylboronic acid in the presence of Pd(PPh3)4 to give an imidazole; reducing II to the aminomethyl analog followed by di-N-alkylation using acyl chlorides and LiAlH4. These compds. may be used for the treatment or prophylaxis of diseases related to the N-methyl-D-aspartate (NMDA)-receptor-subtype selective blockers. Such diseases include acute forms of neurodegeneration caused, e.g., by stroke or brain trauma; chronic forms of neurodegeneration such as Alzheimer's disease, Parkinson's disease, Huntington's disease or ALS (amyotrophic lateral sclerosis); neurodegeneration assocd. with bacterial or viral infections, and diseases such as schizophrenia, anxiety, **depression** and acute/chronic pain.

IT **110-89-4**, Piperidine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(triazole and imidazole derivs., methods of prepn. and use in treatment or prophylaxis of diseases caused by overactivation of resp. NMDA receptor subtypes)

RN 110-89-4 CAPLUS

CN Piperidine (7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L49 ANSWER 21 OF 31 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:861662 CAPLUS
DOCUMENT NUMBER: 134:29325
TITLE: Preparation of metabotropic glutamate receptor

antagonists and their use for treating central nervous system diseases

INVENTOR(S): Van Wagenen, Bradford C.; Moe, Scott T.; Smith, Daryl L.; Sheehan, Susan M.; Shcherbakova, Irina; Travato, Richard; Walton, Ruth; Barmore, Robert; Delmar, Eric G.; Stormann, Thomas M.

PATENT ASSIGNEE(S): NPS Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

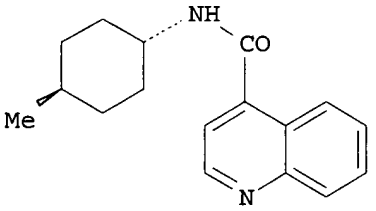
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000073283	A1	20001207	WO 2000-US15222	20000602
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1196397	A1	20020417	EP 2000-936465	20000602
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003500480	T2	20030107	JP 2000-621349	20000602

PRIORITY APPLN. INFO.: US 1999-137272P P 19990602
WO 2000-US15222 W 20000602

OTHER SOURCE(S): MARPAT 134:29325

GI



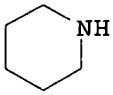
I

AB Title compds. [R1NHCOR; R = quinolinyl, quinoxalinyl, thiazolidinyl, Ph, benzimidazoyl, pyridyl, naphthyridinyl; R1 = phenylpropyl, cyclopentyl, pentyl, cyclohexyl, quinolinyl], stereoisomers, and **pharmaceutically** acceptable salts are prepd. and are active as metabotropic glutamate receptor antagonists (no data). Title compds. are useful for treating neurol. diseases and disorders in **pharmaceutical** compns. Thus, the title compd. I was prepd. for treating disease assocd. with glutamate-induced neuronal damage.

IT **110-89-4**, Piperidine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of mGluR antagonists for treating central nervous system diseases)

RN 110-89-4 CAPLUS

CN Piperidine (7CI, 8CI, 9CI) (CA INDEX NAME)



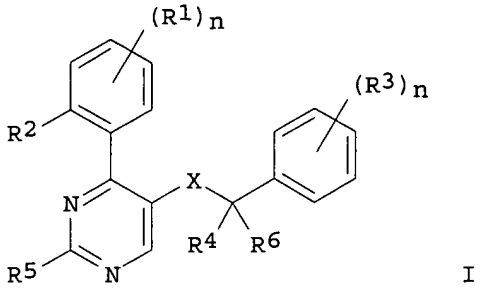
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L49 ANSWER 22 OF 31 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:861658 CAPLUS
DOCUMENT NUMBER: 134:29425
TITLE: Novel 4-phenyl-pyrimidine derivatives as NK-1 receptor antagonists
INVENTOR(S): Boes, Michael; Galley, Guido; Godel, Thierry; Hoffmann, Torsten; Hunkeler, Walter; Schnider, Patrick; Stadler, Heinz
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000073279	A1	20001207	WO 2000-EP4701	20000524
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6274588	B1	20010814	US 2000-575382	20000522
BR 2000011127	A	20020219	BR 2000-11127	20000524
EP 1187815	A1	20020320	EP 2000-927234	20000524
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003500478	T2	20030107	JP 2000-621345	20000524
NO 2001005700	A	20011122	NO 2001-5700	20011122

PRIORITY APPLN. INFO.: EP 1999-110483 A 19990531
WO 2000-EP4701 W 20000524

OTHER SOURCE(S): MARPAT 134:29425
GI



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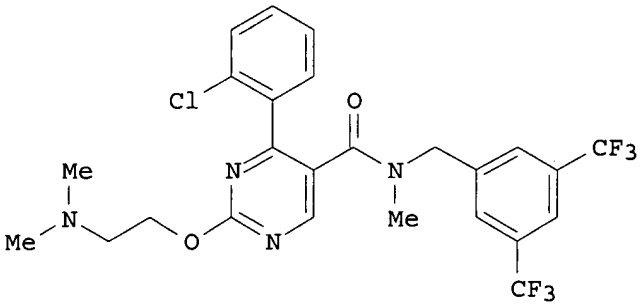


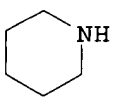
II

AB The invention discloses pyrimidine derivs. I [R1 = H or halo; R2 = H, halo, lower alkyl or lower alkoxy; R1 and R2 may be together with the two carbon atoms -CH=CH-CH=CH-; R3 = halo, CF3, lower alkyl or lower alkoxy; R4, R6 = (independently) H or lower alkyl; R5 = lower alkyl, lower alkoxy, amino, Ph, hydroxy-lower alkyl, cyano-lower alkyl, carbamoyl-lower alkyl, pyridyl, pyrimidyl, (un)substituted -(CH2)n-piperazinyl, which is optionally substituted by one or two lower alkyl groups or by hydroxy-lower alkyl, -(CH2)n-morpholinyl, -(CH2)n-piperidinyl, -(CH2)n+1-imidazolyl, lower alkyl-sulfanyl, lower alkyl-sulfonyl, benzylamino, -NH-(CH2)n+1N(R7)2, -(CH2)n+1N(R7)2, -O-(CH2)n+1-morpholinyl, -O-(CH2)n+1-piperidinyl or -O-(CH2)n+1N(R7)2, wherein R7 = H or lower alkyl; n = 0-2; X = -C(O)N(R7)- or -N(R7)C(O)-] and their **pharmaceutically** acceptable acid addn. salts as NK-1 receptor antagonists. The preferred compds. exhibited pKi values for NK-1 receptor affinity in the range of 8.00-9.20, e.g., the pKi of II was 8.45. With demonstrated affinity to the NK-1 receptor, these compds. may prove useful for the treatment of medical conditions related to this receptor, e.g., inflammatory conditions such as arthritis, migraine, asthma, etc., and in particular CNS disorders such as **depression** or emesis.

IT **110-89-4**, Piperidine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn and biol. activity of phenylpyrimidine derivs. as NK-1 antagonists)

RN 110-89-4 CAPLUS

CN Piperidine (7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L49 ANSWER 23 OF 31 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:772614 CAPLUS
DOCUMENT NUMBER: 133:335165
TITLE: 2-Aminoquinolinecarboxamides: neurokinin receptor ligands
INVENTOR(S): Yuan, Jun; Maynard, George; Hutchison, Alan
PATENT ASSIGNEE(S): Neurogen Corporation, USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000064877	A1	20001102	WO 2000-US11187	20000426
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6369053	B1	20020409	US 2000-560160	20000428
US 2002156095	A1	20021024	US 2002-115409	20020403

PRIORITY APPLN. INFO.: US 1999-131025P P 19990426
US 2000-560160 A1 20000428
OTHER SOURCE(S): MARPAT 133:335165
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. I (X = O, S or N-CN; R1 = H, halo, OH, NO2, CN, SO2NH2, C1-6alkyl, OC1-6alkyl, SO2NHC1-6alkyl, N(C1-6alkyl)2, etc. where C1-6alkyl may be (un)substituted, branched, cyclic, or unsatd.; R2 or R3 = H, halo, OH, NO2, CN, SO2NH2, (un)substituted aryl [aryl may be Ph, naphthyl, thienyl, etc.], C1-8alkyl, OC1-8alkyl, SO2NHC1-8alkyl, N(C1-8alkyl)2, etc. where C1-8alkyl may be (un)substituted, branched, cyclic, or unsatd.; R4 or R5 = independently Q1 or Q2 where R7 = H or C1-8alkyl as defined above and R8 or R9 = H, C1-8alkyl as defined above, aldehyde, ketone, amide, sulfonamide, (un)substituted aryl [aryl may be Ph, naphthyl, thienyl, etc.] or R8R9 join to form a 4-8 membered monocyclic or bicyclic ring [which may contain unsaturations, heteroatoms or R1]) and their **pharmaceutically** acceptable salts or **pharmaceutically** acceptable solvates thereof are disclosed as neurokinin receptor ligands. Thus, compd. II was prepd. by substitution of the corresponding 2-bromo quinoline deriv. with pyrrolidine. As ligands of neurokinin receptors, in particular NK-3 receptors, the compds. disclosed (no data) are useful in the treatment of a wide range of diseases or disorders including, but not limited to **depression**, anxiety, psychosis, obesity, pain, Parkinson's disease, Alzheimer's disease, neurodegenerative diseases, movement disorders, respiratory diseases, inflammatory diseases, neuropathy, immune disorders, migraine, biliary disfunction, and dermatitis.

IT **110-89-4**, Piperidine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn of aminoquinolinecarboxamides as neurokinin receptor antagonists)

RN 110-89-4 CAPLUS

DERWENT-ACC-NO: 2001-159528
DERWENT-WEEK: 200236

TITLE: Melanin-concentrating hormone receptor polypeptides for increasing or decreasing appetite, reducing stress and to screen for compounds that bind to the receptor

INVENTOR: HOWARD, A D

PATENT-ASSIGNEE: MERCK & CO INC[MERI]

PRIORITY-DATA: 1999US-143706P (July 14, 1999)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 200105947 A1	January 25, 2001	E	043	C12N 005/10
EP 1200560 A1	May 2, 2002	E	000	C12N 005/10

DESIGNATED-STATES: CA JP US AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT S
E AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

APPLICATION-DATA:

PUB-NO	APPL-DESCRIPTOR	APPL-NO	APPL-DATE
WO 200105947A1	N/A	2000WO-US18733	July 10, 2000
EP 1200560A1	N/A	2000EP-0947155	July 10, 2000
EP 1200560A1	Based on	WO 200105947	N/A

EP 1200560A1

INT-CL (IPC): C12N005/10; C12N015/12 ; C12N015/63

ABSTRACTED-PUB-NO: WO 200105947A
BASIC-ABSTRACT: NOVELTY - A melanin-concentrating hormone (MCH) receptor polypeptide (I) (free of associated proteins) encoding for at least 9 contiguous amino acids of a sequence (S1) of 69 amino acids defined in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a purified nucleic acid (II) comprising a nucleotide sequence encoding at least 5 contiguous amino acids of (S1);

(2) an expression vector (III) comprising (II);

(3) a recombinant cell (IV) comprising (III);

(4) preparation of MCH receptor polypeptide by growing (IV) and recovering the expressed polypeptide;

(5) a purified nucleic acid comprising a region of 20 contiguous nucleotides, where at least 16 nucleotides present in the region hybridize to a complementary region of 20 contiguous nucleotides present in a sequence (S2) of 207 base pairs defined in the specification or its complement;

(6) screening (V) for a compound able to bind a MCH receptor, by expressing MCH receptor polypeptide or its fragments, providing to the polypeptide a test preparation comprising one or more test compounds and measuring the ability of the test preparation to bind to the polypeptide;

(7) screening (VI) for a compound able to modulate MCH receptor activity, by contacting a cell line expressing a recombinant nucleic acid encoding for a MCH receptor polypeptide with a test preparation comprising one or more test compounds and measuring the effect of the preparation on the

activity of the
receptor; and

(8) suppressing (VII) appetite, by administering a nucleic acid for decreasing
MCH receptor expression by targeting a nucleic acid region within (S2).

ACTIVITY - Cytostatic; Antidiabetic; Tranquilizer; Analgesic.

No supporting data is given.

MECHANISM OF ACTION - Gene therapy.

USE - MCH receptor fragments and polypeptides are useful in assays to screen
for compounds that bind to the MCH receptor and modulate the activity of the
receptor. MCH Receptor activity is modulated to achieve weight loss, weight
gain, to treat cancer (e.g. colon or breast), reduce pain, treat diabetes,
reduce stress or treat sexual dysfunction. Nucleic acid coding for the MCH
receptor can be used to cause an increase in appetite and to create a test
system (e.g. a transgenic animal) for screening for compounds affecting MCH
receptor expression. Inhibition of MCH receptor nucleic acid activity is
useful to inhibit appetite or stress.

CHOSEN-DRAWING: Dwg.0/0

TITLE-TERMS:
MELANIN CONCENTRATE HORMONE RECEPTOR INCREASE DECREASE
APPETITE REDUCE STRESS
SCREEN COMPOUND BIND RECEPTOR

DERWENT-CLASS: B04 D16

CPI-CODES: B04-C01; B04-E03D; B04-F0100E; B04-J01;
B04-K01P0E; B04-N02A0E;
B11-A; B11-C08E1; B12-K04E; B14-C03; B14-D01E; B14-D02B;
B14-H01; B14-J01B4;
B14-L01; B14-L06; B14-S03; D05-C12; D05-H08; D05-H09;
D05-H12A; D05-H12E;
D05-H14; D05-H17A4; D05-H18;

CHEMICAL-CODES:
Chemical Indexing M1 *01*
    Fragmentation Code
    M423 M430 M710 M720 M782 M905 N135 P411 P446 P448
    P633 P711 P731 P816 P831 Q233
    Specfic Compounds
    A00GTT A00GTD A00GTM A00GTN A00GTP

Chemical Indexing M1 *02*
    Fragmentation Code
    M423 M430 M710 M720 M782 M905 N135 P411 P446 P448
    P633 P711 P731 P816 P831 Q233
    Specfic Compounds
    A00H1T A00H1D A00H1M A00H1N A00H1P

Chemical Indexing M1 *03*
    Fragmentation Code
    M423 M430 M710 M720 M782 M905 N135 P411 P446 P448
    P633 P711 P731 P816 P831 Q233
    Specfic Compounds
    A00NST A00NSD A00NSM A00NSN A00NSP

SECONDARY-ACC-NO:
CPI Secondary Accession Numbers: C2001-047449

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
14 December 2000 (14.12.2000)

PCT

(10) International Publication Number
WO 00/75166 A1

(51) International Patent Classification[7]: C07J 14/72, C07H 21/04, C12P 21/02, G01N 33/53, 31/00

(21) International Application Number: PCT/US00/15503

(22) International Filing Date: 6 June 2000 (06.06.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
09/327,807 8 June 1999 (08.06.1999) US

(71) Applicant: THE REGENTS OF THE UNIVERSITY OF CALIFORNIA [US/US]; 1111 Franklin Street, 12th floor, Oakland, CA 94607 (US).

(72) Inventors: CIVELLI, Olivier; 10 Dickens Court, Irvine, CA 92612 (US). SAITO, Yumiko; 3 Gabrielino Drive, Irvine, CA 92612 (US). NOTHACKER, Hans-Peter; 2003 C. Los Trancos Drive, Irvine, CA 92612 (US).

(74) Agent: BERLINER, Robert; Fulbright & Jaworski L.L.P., 29th floor, 865 S. Figueroa Street, Los Angeles, CA 90017-2576 (US).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *With international search report.*
— *With amended claims.*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 00/75166 A1

(54) Title: MELANIN CONCENTRATING HORMONE RECEPTOR

(57) Abstract: The invention provides a method of identifying an MCH receptor agonist or antagonist, by contacting an MCH receptor with one or more candidate compounds under conditions wherein the MCH receptor produces a predetermined signal in response to an MCH receptor agonist, and identifying a compound that alters production of the predetermined signal. The invention also provides a method of identifying an MCH receptor ligand, by contacting an MCH receptor with one or more candidate compounds under conditions that allow selective binding between the MCH receptor and an MCH receptor ligand, and identifying a compound that selectively binds to the MCH receptor. Also provided are methods of identifying an individual having or susceptible to an MCH receptor-associated condition, by detecting MCH receptor nucleic acid or polypeptide in a sample. The invention further provides signaling compositions, which contain a recombinantly expressed MCH receptor and a recombinantly expressed Gα subunit of a G protein, or which contain a recombinantly expressed MCH receptor, a G protein, and a calcium indicator.

DERWENT-ACC-NO: 2001-050021
DERWENT-WEEK: 200119

TITLE: Use of melanin concentrating hormone receptor for identifying MCH
receptor agonist or antagonist, receptor ligand, and an individual susceptible
to the receptor-associated conditions such as memory disorders

INVENTOR: CIVELLI, O; NOTHACKER, H ; SAITO, Y

PATENT-ASSIGNEE: UNIV CALIFORNIA[REGC]

PRIORITY-DATA: 1999US-0327807 (June 8, 1999)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 200075166 A1	December 14, 2000	E	060	C07J 014/72
AU 200058691 A	December 28, 2000	N/A	000	C07H 021/04

DESIGNATED-STATES: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK D
M DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT
LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ
UA UG UZ VN YU ZA ZW AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU M
C MW MZ NL OA PT SD SE SL SZ TZ UG ZW

APPLICATION-DATA:

PUB-NO	APPL-DESCRIPTOR	APPL-NO	APPL-DATE
WO 200075166A1	N/A	2000WO-US15503	June 6, 2000
AU 200058691A	Based on	WO 200075166	June 6, 2000

N/A
AU 200058691A

INT-CL (IPC): C07H021/04; C07J014/72 ; C12P021/02 ;
G01N031/00 ;
G01N033/53

ABSTRACTED-PUB-NO: WO 200075166A
BASIC-ABSTRACT: NOVELTY - Use of MCH (melanin concentrating hormone) receptor
(I) for identifying agonist or antagonist of (I), identifying an MCH receptor
ligand, identifying an individual having or susceptible to (I)-associated
conditions.

DETAILED DESCRIPTION - Use of MCH (melanin concentrating hormone) receptor (I)
for identifying agonist or antagonist of (I), identifying an MCH receptor
ligand, identifying an individual having or susceptible to (I)-associated
conditions.

Identifying an agonist or antagonist of (I) (M1) involves contacting (I) with
one or more candidate compounds under conditions in which (I) produces a
predetermined signal in response to (I) agonist, and identifying a compound
that alters production of the predetermined signal. The compound is then
characterized as (I) agonist or antagonist.

Identifying an individual having or susceptible to (I)-associated condition
(M2) involves detecting MCH receptor nucleic acid molecule or (I) polypeptide
in a sample from an individual. An abnormal structure or expression of the
nucleic acid, or an abnormal expression or activity of (I) polypeptide,
respectively, in the sample indicates that the individual has or is susceptible
to a (I)-associated condition.

Identifying a ligand of (I) (M3) involves contacting (I) with one or more

candidate compounds under conditions that allows selective binding between the
receptor and its ligand and then identifying a compound that selectively binds
to the receptor which is characterized as the ligand of (I).

An INDEPENDENT CLAIM is also included for a signaling composition (SC)
comprising a recombinantly expressed (I) and a recombinantly expressed G alpha
subunit of a G protein. Optionally the composition also includes a calcium
indicator.

ACTIVITY - Anorectic; antiinfertility; immunomodulator; antiparkinsonian;
nootropic; anticonvulsant; neuroprotective; vasotropic; tranquilizer;
antidepressant; neuroleptic; gynecological; contraceptive; osteopathic.

No supporting biological data is given.

MECHANISM OF ACTION - MCH receptor agonist or antagonist.

USE - For identifying agonist or antagonist of (I), identifying an MCH receptor
ligand, identifying an individual having or susceptible to (I)-associated
conditions such as a disorders of body weight (such as disorders involving
increased (obesity) or decreased body weight such as under weight or cachexia),
mood (depression, anxiety disorders, psychotic disorders, schizophrenia),
memory and learning (Alzheimer's disease, dementia, etc.), sleep (insomnia,
bedwetting, sleepwalking, sleep apnea, etc.), dopaminergic system function
(such as Parkinson's disease, Huntington's disease), reproduction (as male or
female contraceptives, or male or female sexual dysfunction, impotence, failure
of lactation, infertility, etc.) or growth (dwarfism or acromegaly) (claimed)
and also disorders of behavior such as autistic disorder, Asperger's disorder
etc. The agonist or antagonist compounds can be used

therapeutically to prevent
or ameliorate (I)-associated conditions as described above. Identifying an
individual having or susceptible to MCH receptor associated conditions allows
optimal medical care for the individual, including appropriate genetic
counseling and prophylactic and therapeutic intervention.

CHOSEN-DRAWING: Dwg.0/5

TITLE-TERMS:
MELANIN CONCENTRATE HORMONE RECEPTOR IDENTIFY RECEPTOR AGONIST ANTAGONIST
RECEPTOR LIGAND INDIVIDUAL SUSCEPTIBILITY RECEPTOR ASSOCIATE CONDITION MEMORY
DISORDER

DERWENT-CLASS: B04 D16 S03

CPI-CODES: B04-B03B; B04-E03D; B04-J01; B04-N02; B05-A01B; B12-K04A; B12-K04E;
B12-K04F; B14-E11; B14-E12; B14-J01; B14-J02; B14-L01; B14-L06; B14-N02;
B14-P01; B14-P02; B14-S02; D05-H09;

EPI-CODES: S03-E09; S03-E14H4;

CHEMICAL-CODES:
Chemical Indexing M1 *01*
    Fragmentation Code
    M423 M750 M905 N102 Q233
    Specfic Compounds
    A00NSK A00NSA

Chemical Indexing M1 *02*
    Fragmentation Code
    M423 M750 M905 N102 Q233
    Specfic Compounds
    A012PK A012PA

Chemical Indexing M1 *03*
    Fragmentation Code
    M423 M430 M750 M781 M782 M905 N102 N135 P831 Q233
    Q505
    Specfic Compounds
    A00H1K A00H1A A00H1D A00H1M